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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,333	11/14/2003	Anastasia Khvorova	DHARMA 0100-US2	6379
23719	7590	09/05/2007		
KALOW & SPRINGUT LLP 488 MADISON AVENUE 19TH FLOOR NEW YORK, NY 10022			EXAMINER EPPS FORD, JANET L	
			ART UNIT 1633	PAPER NUMBER
			MAIL DATE 09/05/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/714,333

Applicant(s)

KHVOROVA ET AL.

Examiner

Janet L. Epps-Ford

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,38-54 and 57-87 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,38-54 and 57-87 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

1. The previously indicated allowability of claims 1, 38-42, 61-78, and 80-83 is withdrawn in view of the new grounds of rejection set forth below.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claim 1, 38-54, and 57-87 are rejected under 35 U.S.C. 102(a or e) as being anticipated by Tuschl et al. (WO 02/44321 A1).

Tuschl et al. discloses the following synthesized siRNA duplex structures (sense on top/antisense on bottom) targeting luciferase in part E of Figure 11, the bar graph shows the normalized relative luminescence of target luciferase to control luciferase in *D. melanogaster* embryo lysate:

E

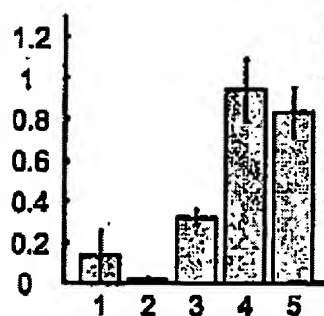
5' AUCACGUAUCCGCGUACGUGAUG3'
GUAUGCAUUGCCCUUAUGAA 5'

5' UCACGUAUCCGCGUACGUGAUG3'
GUAUGCAUUGCCCUUAUGAA 5'

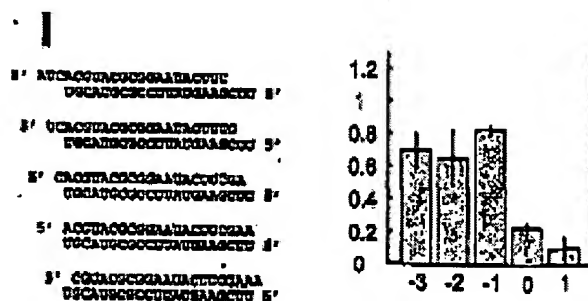
5' CACGUAUCCGCGUACGUGAUG3'
GUAUGCAUUGCCCUUAUGAA 5'

5' ACGUAUCCGCGUACGUGAUG3'
GUAUGCAUUGCCCUUAUGAA 5'

5' CGUAUCCGCGUACGUGAUG3'
GUAUGCAUUGCCCUUAUGAA 5'



In the first siRNA duplex above the antisense region comprises the following sequence: 5'AAGUAUUCCGCGUACGUGAUG3'. The antisense region of this siRNA comprises a structure wherein the total number of A or U residues in the first five, the first four, and the first two nucleotides at the 5' end of the antisense region is higher than that set forth in the last five, the last four, and the last two nucleotides at the 3' end of the molecule. Moreover, the first 5' position of the antisense region has either an A or U nucleotide and the last 3' position of the antisense region has neither an A nor U nucleotide. Additionally, the antisense region includes the presence of U at position 6, the absence of A at position 15, the absence of G at position 1, and the absence of C at position 7 of the antisense sequence. This sequence comprises a GC content between about 30% and 52%, and has at least 2 A or U bases at position 1-5 of the antisense sequence. It is noted that normalized ratios less than 1 indicate specific interference. In the above bar graph, the first duplex comprising a single nucleotide overhang (#1) effectively reduces the relative luminescence of the target luciferase gene.



In part I of Figure 11, the last siRNA duplex above comprises and antisense region having the following nucleotide structure: 5'-UUCGAAGUAUCCGCGUACGU-3'. This siRNA comprises an antisense region wherein there is a higher number of A or U nucleotides in the first 3 nucleotides of the 5' end in comparison to the last 3 nucleotides of the 3' end. This antisense region also comprises a U nucleotide at positions 1, and 17, and includes the absence of U at position 9, the absence of A at position 15, the absence of G at position 1, and the absence of C at position 7. Moreover, this antisense region comprises wherein there are at least 2A or U bases at positions 1-5 of the antisense region, and possesses a GC content of between about 30% and 52%. This siRNA duplex also effective reduces the relative luminescence of the target luciferase gene.

Additionally, Tuschl et al. describes an siRNA duplex having the following sequence (sense at top/antisense at bottom), see Figure 13B:

1' GCGTACGCGGAAATGCTT
3' UGCATGCGCGGAAATGCTT

This sequence comprises a U residue at position 1, an A residue at position 10, includes the absence of C at position 7, the absence of A at position 15, the absence of G at position 1, and has between about 30% and 52% GC content. This siRNA duplex

meets multiple criteria for selecting siRNA as set forth in the instant claims. Moreover, all of the above antisense sequences are described in the reference as being complementary to a luciferase gene mRNA target.

***Reference of Interest
Not prior Art***

4. Elbashir et al. (2002) describes rules useful for designing siRNA molecules. In particular, the design process is drawn to a target site characteristic. At page 202 of this reference, Elbashir et al. discloses the following strategy for identifying regions in an mRNA target for designing siRNA:

Search for sequences 5'-AA(N19)UU, where N is any nucleotide, in the mRNA sequence and choose those with approximately 50% G/C content (Fig. 2A). Nevertheless, 32 to 79% G/C content has also worked well in our hands. Highly G-rich sequences should be avoided because they tend to form G-quartet structures. If there are no 5'-AA(N19)UU motifs present in the target mRNA, search for 5'-AA(N21) or 5'-NA(N21) (Fig. 2B). Independent of the selection procedure described in Fig. 2, synthesize the sense siRNA as 5'-(N19)TT, and the sequence of the antisense siRNA as 5'-(N'19)TT, where N'19 denotes the reverse complement sequence of N19. N19 and N'19 indicate ribonucleotides; T indicates 2'-deoxythymidine.

This passage describes choosing mRNA target regions comprising the following sequences: 5'AA(N19)UU3', 5'AA(N21)3', or 5'-NA(N21)-3'. This passage further states that independent of the selection procedure in Figure 2, the sense siRNA should be synthesized as 5'-(N19)TT, and the antisense siRNA as 5'-(N19)TT. This reference does not disclose wherein the 5' end of the antisense region of the siRNA duplex comprises a higher number of A or U residues in the first 5 nucleotides than that in the last 5 residues of the 3' end.

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5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE